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     (FILE 'HOME' ENTERED AT 14:37:53 ON 30 MAR 2004)

     FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
     AT 14:38:03 ON 30 MAR 2004
L1        541621 S INSULIN
L2         52924 S ERYTHROPOIETIN
L3         57188 S ERYTHROPOIETIN OR EPO
L4        274027 S CHO OR COS OR BHK OR NAMALWA OR HELA
L5           849 S L1 (L) L2 (L) L3
L6           412 DUP REM L5 (437 DUPLICATES REMOVED)
L7           282 S L6 AND PY<=1998
L8           282 FOCUS L7 1-
L9            93 S L8 AND SERUM?
L10           28 S L8 AND SERUM-FREE
L11           28 SORT L10 PY
L12        10514 S RECOMBINANT HUMAN ERYTHROPOIETIN
L13            2 S L12 (L) L1 (L) L4
L14            2 S L1 (L) L4 (L) L12
                 E MIGUEL C?/AU
L15            1 S E4
L16         2270 S E 12
L17            1 S E12
                 E CARCAGNO C?/AU
L18            4 S E4
L19            4 DUP REM L18 (0 DUPLICATES REMOVED)
L20          122 S L12 (L) L4
L21           65 DUP REM L20 (57 DUPLICATES REMOVED)
L22           65 SORT L21 PY
L23            3 S L22 AND INSULIN
L24            9 S L22 AND (SERUM-FREE OR SERUMFREE)

=> s l24 and insulin
L25            1 L24 AND INSULIN

=> d an ti so au ab pi l25

L25  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1998:261609  CAPLUS
DN   129:104852
TI   Serum-free medium used for production of recombinant
     human erythropoietin
SO   Junshi Yixue Kexueyuan Yuankan (1997), 21(4), 244-246
     CODEN: JYKYEL; ISSN: 1000-5501
AU   Deng, Jixian; Yang, Qin; Cheng, Xun; Li, Lin; Lu, Jianshen
AB   Various additives of serum-free medium suitable to
     CHO cells were screened based on the consumption of medium compns.
     of C2 cells producing recombinant human
     erythropoietin (Rhuepo). Se, Ethanolamine, lipid, various
     vitamins, peptone, insulin, transferrin and some cytokines were
     added in a DMEM:F12 (1:1) medium to constitute the serum-
     free medium named SFM-p. It contained no bovine serum albumin but
     could support the growth and Rhuepo production of C2 cells. Productivity of
     Rhuepo with SFM-p was the same as that with 1% FBS medium in rolling
     bottles. The same studies were conducted in a packed bed bioreactor for
     C2 cells by using SFM-p. The C2 cells were cultured with 5% FBS medium
     for 9 days, then substituted with SFM-p. Cell culture in SFM-p could be
     maintained in a stable condition of Rhuepo production for 20 days in the
     bioreactor. The Rhuepo productivity in a bioreactor was 71.0 mg/(L.d),
     and the culture supernatant contained 28.4 μg/mL of Rhuepo. Glucose
     consumption rate was 21 g per L per day. The highest d. of cells could
     exceed 3.0 x 107 cells/mL, and Rhuepo could be easily separated from the
     culture supernatant. Thus, SFM-p can maintain the growth and
     recombinant human erythropoietin production in
     recombinant C2 cells.
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TI **Recombinant human erythropoietin** with superior in vivo activity production in **CHO** cells

SO Braz. Pedido PI, 18 pp.
CODEN: BPXXDX

IN Paez Meireles, Rolando; Rodriguez Molto, Maria Pilar; Garcia del Barco Herrera, Diana; De la Fuente Garcia, Jose de Jesus; Tamayo, Caridad; Rodriguez Rodriguez, Elsa Maria; Rodrigues Mayon, Alina; Limonta Velazquez, Jose Manuel; Ruiz Hernandez, Odalys; Lopez Perea, Patricia

AB A process for production of human recombinant erythropoietin is disclosed which involves a cell-culture system which allows for production of 3 different batches of product free of serum, merely supplemented with **insulin**, followed by a simple process of purification, which includes a G-25 chromatog. step, an ion exchange (Q-Sepharose FF), hydrophobic interaction chromatog. (Bu TSK) and gel filtration. The recovery of erythropoietin is a process taking 15 days.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI BR 9704975	A	19990525	BR 1997-4975	19971003

L23 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:261609 CAPLUS
DN 129:104852
TI Serum-free medium used for production of recombinant human erythropoietin
SO Junshi Yixue Kexueyuan Yuankan (1997), 21(4), 244-246
CODEN: JYKYEL; ISSN: 1000-5501
AU Deng, Jixian; Yang, Qin; Cheng, Xun; Li, Lin; Lu, Jianshen
AB Various additives of serum-free medium suitable to **CHO** cells were screened based on the consumption of medium compns. of C2 cells producing **recombinant human erythropoietin** (Rhuepo). Se, Ethanolamine, lipid, various vitamins, peptone, **insulin**, transferrin and some cytokines were added in a DMEM:F12 (1:1) medium to constitute the serum-free medium named SFM-p. It contained no bovine serum albumin but could support the growth and Rhuepo production of C2 cells. Productivity of Rhuepo with SFM-p was the same as that with 1% FBS medium in rolling bottles. The same studies were conducted in a packed bed bioreactor for C2 cells by using SFM-p. The C2 cells were cultured with 5% FBS medium for 9 days, then substituted with SFM-p. Cell culture in SFM-p could be maintained in a stable condition of Rhuepo production for 20 days in the bioreactor. The Rhuepo productivity in a bioreactor was 71.0 mg/(L.d), and the culture supernatant contained 28.4 μg/mL of Rhuepo. Glucose consumption rate was 21 g per L per day. The highest d. of cells could exceed 3.0 x 107 cells/mL, and Rhuepo could be easily separated from the culture supernatant. Thus, SFM-p can maintain the growth and **recombinant human erythropoietin** production in recombinant C2 cells.

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     (FILE 'HOME' ENTERED AT 14:37:53 ON 30 MAR 2004)

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L8           282 FOCUS L7 1-
L9            93 S L8 AND SERUM?
L10           28 S L8 AND SERUM-FREE
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L14            2 S L1 (L) L4 (L) L12
                 E MIGUEL C?/AU
L15            1 S E4
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                 E CARCAGNO C?/AU
L18            4 S E4
L19            4 DUP REM L18 (0 DUPLICATES REMOVED)
L20          122 S L12 (L) L4
L21           65 DUP REM L20 (57 DUPLICATES REMOVED)
L22           65 SORT L21 PY
L23            3 S L22 AND INSULIN

=> d an ti so au ab pi l23 1-3

L23  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2000:335522  CAPLUS
DN   132:321013
TI   Method for the massive culture of cells producing recombinant human
     erythropoietin
SO   PCT Int. Appl., 23 pp.
     CODEN: PIXXD2
IN   Carcagno, Carlos Miguel; Criscuolo, Marcelo; Melo, Carlos; Vidal, Juan
     Alejandro
AB   The present invention relates, in general, to a method for the massive
     culture of recombinant mammalian cells for the production of recombinant human
     erythropoietin (EPO) in culture medium containing insulin. The
     present invention also refers to a method of producing EPO and to the EPO
     thus produced.
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 2000027997      A1   20000518       WO 1999-US26240  19991108
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SL, TJ
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     BR 9905868         A    20010123       BR 1999-5868     19990707
     MX 9910043         A    20000930       MX 1999-10043    19991101
     EP 1127104         A1   20010829       EP 1999-958810   19991108
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     JP 2002529072      T2   20020910       JP 2000-581164   19991108

L23  ANSWER 2 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2000:164674  CAPLUS
DN   132:171061
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IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 9905868	A	20010123	BR 1999-5868	19990707
MX 9910043	A	20000930	MX 1999-10043	19991101
EP 1127104	A1	20010829	EP 1999-958810	19991108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002529072	T2	20020910	JP 2000-581164	19991108

L22 ANSWER 62 OF 65 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:312000 CAPLUS
DN 136:320319
TI Expression system for producing **recombinant human erythropoietin** in **BHK**-21 cells, method for purifying secreted erythropoietin using a two-step chromatography and uses thereof
SO U.S., 11 pp.
CODEN: USXXAM
IN Hsu, Li-Wei; Chang, Su-Chen
AB The present invention provides a newly developed expression system of pcDNA3.1 for producing **recombinant human erythropoietin** (hrEPO) in **BHK**-21 cells, and a novel method of purifying the secreted rhEPOs using a two-step column chromatog. technique. Specifically, the invention provides an expression vector containing a cDNA fragment encoding human erythropoietin and pcDNA3.1 vector under the control of cytomegalovirus promoter for producing **recombinant human erythropoietin** (rhEPO) in **BHK**-21 cells exhibiting biol. activity and immunochem. properties of the native human erythropoietin (hEPO). The invention also provides a transformant (**BHK**-21 cell) harboring the expression vector stably producing secretive rhEPO with a high yield under the selection with antibiotic G418. Also provided is an improved two-step column chromatog. method for purifying rhEPO from culture medium by precipitating rhEPO from a sample, applying the precipitated hrEPO to an immobilized lectin column and eluting the hrEPO from a gel filtration column.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6376218	B1	20020423	US 1998-206826	19981207
TW 445295	B	20010711	TW 1997-86120102	19971231
EP 1010758	A2	20000621	EP 1999-116174	19990823
EP 1010758	A3	20011219		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001078770	A2	20010327	JP 1999-239009	19990825
JP 3352429	B2	20021203		
CN 1260398	A	20000719	CN 1999-118997	19990907

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AB The present invention provides an expression system for producing recombinant human erythropoietin (rhEPO) exhibiting biol. activity and immunochem. properties of the native human erythropoietin (hEPO). Also provided is an improved method for purifying rhEPO from culture medium by two-step column chromatog.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1010758	A2	20000621	EP 1999-116174	19990823
EP 1010758	A3	20011219		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6376218	B1	20020423	US 1998-206826	19981207

L22 ANSWER 53 OF 65 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:335586 CAPLUS
DN 132:321018
TI Host cells expressing recombinant human erythropoietin
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
IN Carcagno, Carlos Miguel; Criscuolo, Marcelo; Melo, Carlos; Vidal, Juan Alejandro
AB The gene coding for human erythropoietin (EPO) was obtained from human genomic DNA. The gene used does not include sequences from regions at 5' of the first translated ATG and 3' of the stop codon of the EPO gene. The gene was cloned into an expression plasmid for eukaryotic cells that have as sole expression control elements the early promoter of the SV40 virus and its polyadenylation signal. Recombinant CHO cells resulting from transfection with genetic constructs used provide an unexpectedly high level of protein expression of 50 mg of recombinant EPO per L of culture medium per day. The cloned gene and resultant mRNA were found complete and had the correct sequence for EPO. Anal. of the recombinant EPO showed total homol. to human EPO.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000028066	A1	20000518	WO 1999-US26238	19991108
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9905867	A	20010123	BR 1999-5867	19990707
MX 9910042	A	20000930	MX 1999-10042	19991101
EP 1124984	A1	20010822	EP 1999-971863	19991108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002529100	T2	20020910	JP 2000-581232	19991108

L22 ANSWER 54 OF 65 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:335522 CAPLUS
DN 132:321013
TI Method for the massive culture of cells producing recombinant human erythropoietin
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
IN Carcagno, Carlos Miguel; Criscuolo, Marcelo; Melo, Carlos; Vidal, Juan Alejandro
AB The present invention relates, in general, to a method for the massive culture of recombinant mammalian cells for the production of recombinant human erythropoietin (EPO) in culture medium containing insulin. The present invention also refers to a method of producing EPO and to the EPO thus produced.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000027997	A1	20000518	WO 1999-US26240	19991108
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,				

AN 2000:496474 CAPLUS
DN 133:72997
TI Method of preparing recombinant human erythropoietin by a strain of cultured Chinese hamster ovary cells, a producer of erythropoietin
SO Russ.
From: Izobreteniya 1999, (2), 489-90.
CODEN: RUXXE7
AB Title only translated.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI RU 2125093	C1	19990120	RU 1998-101995	19980212

L22 ANSWER 40 OF 65 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:164674 CAPLUS
DN 132:171061
TI **Recombinant human erythropoietin** with superior in vivo activity production in **CHO** cells
SO Braz. Pedido PI, 18 pp.
CODEN: BPXXDX
IN Paez Meireles, Rolando; Rodriguez Molto, Maria Pilar; Garcia del Barco Herrera, Diana; De la Fuente Garcia, Jose de Jesus; Tamayo, Caridad; Rodriguez Rodriguez, Elsa Maria; Rodrigues Mayon, Alina; Limonta Velazquez, Jose Manuel; Ruiz Hernandez, Odalys; Lopez Perea, Patricia
AB A process for production of human recombinant erythropoietin is disclosed which involves a cell-culture system which allows for production of 3 different batches of product free of serum, merely supplemented with insulin, followed by a simple process of purification, which includes a G-25 chromatog. step, an ion exchange (Q-Sepharose FF), hydrophobic interaction chromatog. (Bu TSK) and gel filtration. The recovery of erythropoietin is a process taking 15 days.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI BR 9704975	A	19990525	BR 1997-4975	19971003

L22 ANSWER 42 OF 65 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:647423 CAPLUS
DN 132:150620
TI High density and high expression culture of recombinant human erythropoietin expressing cell line
SO Zhongguo Shenghua Yaowu Zazhi (1999), 20(3), 116-118
CODEN: ZSYZFP; ISSN: 1005-1678
AU Zou, Zhongcheng; Hu, Ming
AB Purpose: Bioreactor was used for the culture of recombinant erythropoietin expressing CHO cell line, in order to realize high d. and high expression culture. Methods: Expressing cell line was first cultured in flasks with DMEM-F12 medium containing 5% serum. When the total number of the cells reached about 2+108, they were inoculated into the 5 L bioreactor. After 7 days culture with medium containing serum, and the serum free medium was utilized to continue the culture for another 30 days. Based on the growth situation, continuous culture was performed by perfusion method. Glucose concentration was kept above 0.5 g/L. Lactate and ammonia were also measured at the same time to avoid their accumulation. Sample was taken everyday for the anal. of EPO expression in the harvest medium. When the culture was over, 0.25% trypsin was used to digest the carriers, and the total cell number was counted after the cells dropped from the carriers. Results: The cell d. reached 6+106/mL medium, the expression level was about 30 000 IU/mL, and the expressed EPO had a relatively high biol. specific activity. Conclusion: Under adequate culture conditions, high d. and high expression culture of the recombinant cell line could be realized by using bioreactor.

L22 ANSWER 51 OF 65 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:420835 CAPLUS
DN 133:39085
TI An expression system for producing recombinant human erythropoietin, a method for purifying the secreted human erythropoietin and uses thereof
SO Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
IN Hsu, Li-Wei; Chang, Su-Chen

affinity-purified from culture supernatants, and was biologically active in vivo. Based on secretion rates from **BHK**-21 cells, the most potent erythropoietin was rhuEpoGln24. This mutein is also considered to have biologic activities that are superior to rhuEpowt.

L22 ANSWER 23 OF 65 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:672056 CAPLUS
DN 127:326650
TI Secretion of biologically active recombinant human erythropoietin in mammalian cell culture
SO Biotecnologia Aplicada (1995), 12(3), 165-166
CODEN: BTAPEP; ISSN: 0864-4551
AU Garcia del Barco, Diana; Rodriguez, Alina; Rodriguez, Elsa; Tamayo, Caridad; Lleonart, Ricardo; Aguirre, Alina; de la Fuente, Jose
AB **Recombinant human erythropoietin** (hEPO) was detected after transient transfection of **CHO** cells with an expression plasmid containing full length cDNA of hEPO cloned from fetal kidneys. A stable transformed line of **CHO** was established. The rhEPO was partially purified by affinity chromatog. on Blue Sepharose and was detected by either a com. EIA or in immunodots with a rabbit heteroserum against a peptide of hEPO. Purification of rhEPO yielded a reproducible, more than 90% purity product. Thus, the authors achieved secretion of biol. active rhEPO in **CHO** cells.

L22 ANSWER 29 OF 65 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:540363 CAPLUS
DN 129:328771
TI Effect of sodium butyrate on the expression of **recombinant human erythropoietin** in engineered **CHO**-EPO cell line
SO Shengwu Gongcheng Xuebao (1997), 13(3), 269-272
CODEN: SGXUED; ISSN: 1000-3061
AU Liu, Xiaoping; Wang, Yan; Zhu, Kui; Cao, Yunxu; Lu, Deru
AB Various concns. (0.5, 1.0, 2.5 and 5.0 mmol·L-1) of sodium butyrate (NaBut) were added into the serum-free cell culture resp. to increase its erythropoietin (EPO) expression level. NaBut inhibited the engineered cells growth markedly, increased EPO expression within a long period at all concns. except 5.0 mmol·L-1 (1.0 mmol·L-1 was the optimal one), delayed the cells falling off in the serum-free culture, and increased EPO mRNA level.

L22 ANSWER 30 OF 65 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:261609 CAPLUS
DN 129:104852
TI Serum-free medium used for production of recombinant human erythropoietin
SO Junshi Yixue Kexueyuan Yuankan (1997), 21(4), 244-246
CODEN: JYKYEL; ISSN: 1000-5501
AU Deng, Jixian; Yang, Qin; Cheng, Xun; Li, Lin; Lu, Jianshen
AB Various additives of serum-free medium suitable to **CHO** cells were screened based on the consumption of medium compns. of C2 cells producing **recombinant human erythropoietin** (Rhuepo). Se, Ethanolamine, lipid, various vitamins, peptone, insulin, transferrin and some cytokines were added in a DMEM:F12 (1:1) medium to constitute the serum-free medium named SFM-p. It contained no bovine serum albumin but could support the growth and Rhuepo production of C2 cells. Productivity of Rhuepo with SFM-p was the same as that with 1% FBS medium in rolling bottles. The same studies were conducted in a packed bed bioreactor for C2 cells by using SFM-p. The C2 cells were cultured with 5% FBS medium for 9 days, then substituted with SFM-p. Cell culture in SFM-p could be maintained in a stable condition of Rhuepo production for 20 days in the bioreactor. The Rhuepo productivity in a bioreactor was 71.0 mg/(L.d), and the culture supernatant contained 28.4 μg/mL of Rhuepo. Glucose consumption rate was 21 g per L per day. The highest d. of cells could exceed 3.0 x 107 cells/mL, and Rhuepo could be easily separated from the culture supernatant. Thus, SFM-p can maintain the growth and **recombinant human erythropoietin** production in recombinant C2 cells.

L22 ANSWER 39 OF 65 CAPLUS COPYRIGHT 2004 ACS on STN

AU Ohashi, Hideya; Miyata, Miki; Ishii, Yasuyuki; Takeuchi, Makoto; Takasago, Akemi; Suzuki, Takamoto; Sudo, Tadashi
AB The establishment of a transfected **HeLa** cell line producing **recombinant human erythropoietin** (rHuEPO) and some characteristics of rHuEPO derived from **HeLa** cells are described. **HeLa** cells were found to be suitable as a host cell line for the production of recombinant glycoproteins.

L22 ANSWER 12 OF 65 MEDLINE on STN
AN 93290841 MEDLINE
TI In vivo biological activities of **recombinant human erythropoietin** analogues produced by **CHO** cells, **BHK** cells and C127 cells.
SO Biologicals : journal of the International Association of Biological Standardization, (1992 Dec) 20 (4) 253-7.
Journal code: 9004494. ISSN: 1045-1056.
AU Hayakawa T; Wada M; Mizuno K; Abe S; Miyashita M; Ueda M
AB The in vivo biological activity of four pharmaceutical preparations of **recombinant human erythropoietin** was compared. Two of the erythropoietins were produced by Chinese hamster ovary cells, **CHO**-K1, and the others were produced by mouse mammary cells, C127, and baby hamster kidney cells, **BHK**-21. The activities of the analogues were estimated by a simple cell counting method with conventional automated microcell counters. The amounts of these analogues gave straight logarithmic dose-response curves when plotted against the count of particles resistant to hemolysing reagent, which particles were mostly immature reticulocytes. The lines from the four analogues were parallel to each other. The relative activities of these analogues were 1.02, 1.19 and 1.21 when one of the analogues was arbitrarily used as the standard. These differences in the extent of the activity were not significant. Thus, the four **recombinant human erythropoietin** analogues, produced by four different mammalian cell lines, expressed the same biological potencies in vivo corresponding to their units, and the units used up to now by the manufacturers are equivalent. These results also draw the conclusion that the new simple in vivo bioassay can replace the existing accepted assay methods.

L22 ANSWER 20 OF 65 MEDLINE on STN
AN 95300975 MEDLINE
TI Identification and structural characterization of a mannose-6-phosphate containing oligomannosidic N-glycan from human erythropoietin secreted by recombinant BHK-21 cells.
SO FEBS letters, (1995 May 29) 365 (2-3) 203-8.
Journal code: 0155157. ISSN: 0014-5793.
AU Nimtz M; Wray V; Rudiger A; Conradt H S
AB A sialidase resistant mono-charged N-glycan was isolated from glycosylation site I (Asn-24) of **recombinant human erythropoietin** expressed from baby hamster kidney (**BHK** -21) cells and constituted approximately 2-4% of the oligosaccharide material at this glycosylation site. Mass spectrometry and both 1- and 2-dimensional NMR techniques revealed a high mannose type structure (Man6) with a phospho-diesterbridged N-acetylglucosamine as follows: [formula: see text]

L22 ANSWER 22 OF 65 MEDLINE on STN
AN 95161746 MEDLINE
TI N- and O-glycosylation muteins of **recombinant human erythropoietin** secreted from **BHK**-21 cells.
SO Blood, (1995 Mar 1) 85 (5) 1229-36.
Journal code: 7603509. ISSN: 0006-4971.
AU Fibi M R; Hermentin P; Pauly J U; Lauffer L; Zettlmeissl G
AB Single-site glycomuteins of **recombinant human erythropoietin** (rhuEpo) were constructed and transiently and stably expressed in **BHK**-21 cells. The transient expression levels varied among muteins, being highest for mutein rhuEpoGln24 followed by wild-type rhuEpo (rhuEpowt). All other glycomuteins, including rhuEpoGln38, rhuEpoGln83, rhuEpoThr126, and rhuEpoGly126, were secreted at lower levels than rhuEpowt. Muteins expressed in stable cell lines showed similar differences in expression levels. Also each mutein could be

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(FILE 'HOME' ENTERED AT 14:37:53 ON 30 MAR 2004)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 14:38:03 ON 30 MAR 2004

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L1        541621 S INSULIN
L2         52924 S ERYTHROPOIETIN
L3         57188 S ERYTHROPOIETIN OR EPO
L4        274027 S CHO OR COS OR BHK OR NAMALWA OR HELA
L5           849 S L1 (L) L2 (L) L3
L6           412 DUP REM L5 (437 DUPLICATES REMOVED)
L7           282 S L6 AND PY<=1998
L8           282 FOCUS L7 1-
L9            93 S L8 AND SERUM?
L10           28 S L8 AND SERUM-FREE
L11           28 SORT L10 PY
L12        10514 S RECOMBINANT HUMAN ERYTHROPOIETIN
L13            2 S L12 (L) L1 (L) L4
L14            2 S L1 (L) L4 (L) L12
                 E MIGUEL C?/AU
L15            1 S E4
L16         2270 S E 12
L17            1 S E12
                 E CARCAGNO C?/AU
L18            4 S E4
L19            4 DUP REM L18 (0 DUPLICATES REMOVED)
L20          122 S L12 (L) L4
L21           65 DUP REM L20 (57 DUPLICATES REMOVED)
L22           65 SORT L21 PY
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=> d an ti so au ab pi l22 7 9 11 12 20 22 23 29 30 39 40 42 51 53 54 62

L22 ANSWER 7 OF 65 MEDLINE on STN
AN 89377480 MEDLINE
TI **Recombinant human erythropoietin** produced by **Namalwa** cells.
SO DNA (Mary Ann Liebert, Inc.), (1989 Jul-Aug) 8 (6) 419-27.
Journal code: 8302432. ISSN: 0198-0238.
AU Yanagi H; Yoshima T; Ogawa I; Okamoto M
AB To establish a practical exogenous gene expression system in human cells, a cDNA coding for human erythropoietin (EPO) was expressed in human B-lymphoblastoid Namalwa cells. The Namalwa-derived recombinant EPO was purified from the culture fluid by a simple three-step procedure. The Namalwa EPO showed an equivalent activity in vivo to that of human urinary EPO. Oligosaccharide structure analyses suggested that almost all N-linked oligosaccharide chains of Namalwa EPO are shared by urinary EPO. The two major N-linked oligosaccharides of Namalwa EPO were fucose-containing tetraantennary and fucose-containing triantennary structures.

L22 ANSWER 9 OF 65 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
AN 89:406145 SCISEARCH
TI **RECOMBINANT HUMAN ERYTHROPOIETIN** PRODUCED BY **NAMALWA** CELLS
SO DNA-A JOURNAL OF MOLECULAR & CELLULAR BIOLOGY, (1989) Vol. 8, No. 6, pp. 419-427.
AU YANAGI H (Reprint); YOSHIMA T; OGAWA I; OKAMOTO M

L22 ANSWER 11 OF 65 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:524676 CAPLUS
DN 117:124676
TI Purification and characterization of **recombinant human erythropoietin** expressed in human cervix carcinoma **HeLa** cells
SO Trends Anim. Cell Cult. Technol., Proc. Annu. Meet. Jpn. Assoc. Anim. Cell Technol., 2nd (1990), Meeting Date 1989, 115-20. Editor(s): Murakami, Hiroki. Publisher: Kodansha, Tokyo, Japan.
CODEN: 58ADAS

JP 2002529072 T2 20020910 JP 2000-581164 19991108

L19 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:335432 CAPLUS
DN 132:352760
TI Methods of purifying recombinant human erythropoietin from cell culture supernatants
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
IN **Carcagno, Carlos Miguel**; Criscuolo, Marcelo; Melo, Carlos; Vidal, Juan Alejandro
AB The present invention relates, in general, to a method of purifying recombinant human erythropoietin (EPO). The present invention also relates to a substantially pure EPO. The method comprises a differential precipitation, an hydrophobic interaction chromatog., various concentration and diafiltration steps, tandem anionic and cationic exchange chromatogs. and mol. exclusion chromatog. for the obtaining of pure EPO. The method does not comprise high performance liquid chromatog. steps. The invention also comprises the EPO obtained according to the claimed procedure.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000027869	A1	20000518	WO 1999-US26241	19991108
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9917606	A	20021231	BR 1999-17606	19990707
MX 9910045	A	20000930	MX 1999-10045	19991101
EP 1127063	A1	20010829	EP 1999-958811	19991108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002529475	T2	20020910	JP 2000-581046	19991108

L19 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:335260 CAPLUS
DN 132:352795
TI Method for obtaining lyophilized pharmaceutical compositions of recombinant human erythropoietin stable at room temperature
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
IN **Carcagno, Carlos Miguel**; Criscuolo, Marcelo; Melo, Carlos; Vidal, Juan Alejandro
AB The present invention relates, in general, to a lyophilized pharmaceutical composition comprising recombinant human erythropoietin, which retains at least 95 % of its biol. activity after 24 mo at room temperature The present invention also relates to a method for producing a recombinant human erythropoietin compound, which is stable at room temperature

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000027419	A1	20000518	WO 1999-US26237	19991108
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
MX 9910044	A	20000930	MX 1999-10044	19991101
BR 2001007531	A	20030826	BR 2001-7531	20011218

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L19 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:335586 CAPLUS
DN 132:321018
TI Host cells expressing recombinant human erythropoietin
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
IN **Carcagno, Carlos Miguel**; Criscuolo, Marcelo; Melo, Carlos; Vidal, Juan Alejandro
AB The gene coding for human erythropoietin (EPO) was obtained from human genomic DNA. The gene used does not include sequences from regions at 5' of the first translated ATG and 3' of the stop codon of the EPO gene. The gene was cloned into an expression plasmid for eukaryotic cells that have as sole expression control elements the early promoter of the SV40 virus and its polyadenylation signal. Recombinant CHO cells resulting from transfection with genetic constructs used provide an unexpectedly high level of protein expression of 50 mg of recombinant EPO per L of culture medium per day. The cloned gene and resultant mRNA were found complete and had the correct sequence for EPO. Anal. of the recombinant EPO showed total homol. to human EPO.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000028066	A1	20000518	WO 1999-US26238	19991108
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9905867	A	20010123	BR 1999-5867	19990707
MX 9910042	A	20000930	MX 1999-10042	19991101
EP 1124984	A1	20010822	EP 1999-971863	19991108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002529100	T2	20020910	JP 2000-581232	19991108

L19 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:335522 CAPLUS
DN 132:321013
TI Method for the massive culture of cells producing recombinant human erythropoietin
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
IN **Carcagno, Carlos Miguel**; Criscuolo, Marcelo; Melo, Carlos; Vidal, Juan Alejandro
AB The present invention relates, in general, to a method for the massive culture of recombinant mammalian cells for the production of recombinant human erythropoietin (EPO) in culture medium containing insulin. The present invention also refers to a method of producing EPO and to the EPO thus produced.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000027997	A1	20000518	WO 1999-US26240	19991108
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9905868	A	20010123	BR 1999-5868	19990707
MX 9910043	A	20000930	MX 1999-10043	19991101
EP 1127104	A1	20010829	EP 1999-958810	19991108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

growth and **recombinant human erythropoietin** production in recombinant C2 cells.

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     (FILE 'HOME' ENTERED AT 14:37:53 ON 30 MAR 2004)

     FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
     AT 14:38:03 ON 30 MAR 2004
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L6           412 DUP REM L5 (437 DUPLICATES REMOVED)
L7           282 S L6 AND PY<=1998
L8           282 FOCUS L7 1-
L9            93 S L8 AND SERUM?
L10           28 S L8 AND SERUM-FREE
L11           28 SORT L10 PY
L12        10514 S RECOMBINANT HUMAN ERYTHROPOIETIN
L13            2 S L12 (L) L1 (L) L4
L14            2 S L1 (L) L4 (L) L12

=> d an ti so au ab pi l14 1-2

L14  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2000:164674  CAPLUS
DN   132:171061
TI   Recombinant human erythropoietin with superior in vivo activity production
     in CHO cells
SO   Braz. Pedido PI, 18 pp.
     CODEN: BPXXDX
IN   Paez Meireles, Rolando; Rodriguez Molto, Maria Pilar; Garcia del Barco
     Herrera, Diana; De la Fuente Garcia, Jose de Jesus; Tamayo, Caridad;
     Rodriguez Rodriguez, Elsa Maria; Rodrigues Mayon, Alina; Limonta
     Velazquez, Jose Manuel; Ruiz Hernandez, Odalys; Lopez Perea, Patricia
AB   A process for production of human recombinant erythropoietin is disclosed
     which involves a cell-culture system which allows for production of 3
     different batches of product free of serum, merely supplemented with
     insulin, followed by a simple process of purification, which includes a G-25
     chromatog. step, an ion exchange (Q-Sepharose FF), hydrophobic interaction
     chromatog. (Bu TSK) and gel filtration.  The recovery of erythropoietin is
     a process taking 15 days.
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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PI   BR 9704975         A    19990525       BR 1997-4975     19971003

L14  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1998:261609  CAPLUS
DN   129:104852
TI   Serum-free medium used for production of recombinant human erythropoietin
SO   Junshi Yixue Kexueyuan Yuankan (1997), 21(4), 244-246
     CODEN: JYKYEL; ISSN: 1000-5501
AU   Deng, Jixian; Yang, Qin; Cheng, Xun; Li, Lin; Lu, Jianshen
AB   Various additives of serum-free medium suitable to CHO cells
     were screened based on the consumption of medium compns. of C2 cells
     producing recombinant human erythropoietin
     (Rhuepo).  Se, Ethanolamine, lipid, various vitamins, peptone,
     insulin, transferrin and some cytokines were added in a DMEM:F12
     (1:1) medium to constitute the serum-free medium named SFM-p.  It
     contained no bovine serum albumin but could support the growth and Rhuepo
     production of C2 cells.  Productivity of Rhuepo with SFM-p was the same as
     that with 1% FBS medium in rolling bottles.  The same studies were
     conducted in a packed bed bioreactor for C2 cells by using SFM-p.  The C2
     cells were cultured with 5% FBS medium for 9 days, then substituted with
     SFM-p.  Cell culture in SFM-p could be maintained in a stable condition of
     Rhuepo production for 20 days in the bioreactor.  The Rhuepo productivity in a
     bioreactor was 71.0 mg/(L.d), and the culture supernatant contained 28.4
     μg/mL of Rhuepo.  Glucose consumption rate was 21 g per L per day.  The
     highest d. of cells could exceed 3.0 x 107 cells/mL, and Rhuepo could be
     easily separated from the culture supernatant.  Thus, SFM-p can maintain the
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L8 ANSWER 3 OF 282 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:18879 CAPLUS
DN 118:18879
TI Serum-free medium for cultivation of mammalian cells
SO Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
IN Koch, Stefan; Behrendt, Ulrich; Franze, Rienhard; Lorenz, Thomas; Szperalski, Berthold
AB The title medium, which contains no proteins of animal origin, contains recombinant **insulin** from a prokaryote and a water-soluble Fe compound in place of the animal **insulin** and transferrin used in conventional serum-free media. The medium may be used for cultivation of recombinant CHO cells containing an **erythropoietin** gene for production of **erythropoietin**. Thus, a medium for CHO cells was prepared by mixing equal vols. of Dulbecco's modified Eagle's medium and Nutrient Mixture F-12 and adding biotin 0.2036, recombinant **insulin** 5.0, putrescine 0.1, vitamin B12 0.78, Fe citrate 124 mg/L, hydrocortisone 3.6 μg/L, and poly(vinyl alc.) 1 g/L. The maximum viable and total cell densities achieved were 15.3 + 10-5 and 25.7 + 10-5/mL, resp., both after 164 h.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 513738	A2	19921119	EP 1992-107997	19920512	<--
	EP 513738	A3	19930505			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE					
	DE 4115722	A1	19921119	DE 1991-4115722	19910514	<--
	JP 05252942	A2	19931005	JP 1992-117275	19920511	<--